Comparative study between anti-ccp and rheumatoid factor as diagnostic value of rheumatoid arthritis patients

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Abstract

Objectives
Rheumatoid arthritis disease is an autoimmune infirmity disease. For avoiding the damage of joint and organ, early diagnosis and early treatment are the superior means. This study aimed to compare between ACCP (anti-cyclic citrullinated peptide antibody) and rheumatoid factor (RF) as the diagnostic value of rheumatoid arthritis patients (RA).

Method
This study carried out on RA patients, who clinically diagnostic, were admitted at the physical medicine and rehabilitation clinics of Al-Sader Teaching Hospital between December 2017 and February 2018 prospectively. The protocol of the current study was approved by the medical ethics of Ministry of Health and Environment according to the American Rheumatism Association. By using ELISA kit Anti-CCP and RF were determined. A total of 207 serum samples was collected from RA patients, which consist of 86 males and 121 females. At the same time, a total of 93 serum samples was collected from non-RA persons (control), which consist of 42 males and 51 females. SPSS (version 17.0) was used for statistical analysis; T-test was used to test whether there is a different between non-RA and RA groups. Also, RA correlation with Anti-chip was tested.

Results
The results showed that there was a positive correlation between values of ACCP Log10 and RF Log10 of male and female patients (P-value <0.01). The statistical analysis showed that there was a difference in anti-cyclic citrullinated peptide antibody and rheumatoid factor among the groups of study and all controls were negative for ACCP.

Conclusions
We concluded ACCP (anti-cyclic citrullinated peptide antibody) is a good indicator for RA diagnosis as compared with rheumatoid factor (RF).

Keywords: Anti-CCP, rheumatoid arthritis, rheumatoid factor


Introduction
Rheumatoid arthritis (RA) is an inflammatory autoimmune disease for long-life that affects joints primarily causing pain, stiffness and difficulty in movements. Cartilages, synovial cells, and some systems of the body are affected with autoimmunity and inflammatory processes of RA [1-2]. Early discovery, diagnosis, and treatment are the superior means to bypass the joint demolition, organ hurt, and its incompetence [3-6], on the other hand, an early-accurate diagnosis of RA may protect others who do not have it [7]. Over 50 years ago, Rheumatoid factor (RF) was identified in RA patients [8]. RF value as a diagnostic tool is suboptimal, although it is still as one of the classification criteria of the Rheumatology American College for RA, due to its lack of specificity [9-10]. For diagnosis “of most” of the chronic diseases, there is a very specific standard test, while there is no such specific laboratory test for RA diagnosis. The classification criterion to define RA that is used internationally was defined by the ACR [11]. Nienhuis et al [12] discovered the Citrullinated binding auto-antibodies in RA patients and called anti-per nuclear factoring. Youngs et al[13] notified that the sera of RA contained antibodies could interact with the layer of keratinized of epithelial cell called anti-keratin antibodies present in RA patients only, and in 2002 [14] has discovered the first test of ACCP, which associated with these antibodies. While Van Venrooij et al [15] developed the test of ACCP. The high specificity of the checking still needs more deeply studies, so this study comes to assess anti-CCP and RF in a different gender group of patients compared with control and to study the relationship between RA levels and immune globulin groups.
Methods

This study carried out on RA patients, who were clinically diagnosed, were admitted at the physical medicine and rehabilitation clinics of Al-Sader Teaching Hospital between December 2017 and February 2018 prospectively. The protocol of the current study was approved by the medical ethics of Ministry of Health and Environment, according to the American Rheumatism Association [11], RA was diagnosed by using an ELISA kit (EDRA Genesis Diagnostics, Cambridgeshire, UK), Anti-CCP was determined. A total of 207 serum samples was collected from RA patients, which consist of 86 males and 121 females were between 18 to 77 (mean = 43, standard deviation= ± 14) years old. In the same time, a total of 93 serum samples were collected from non-RA persons (control), which consist of 42 males were between 21 to 66 years old and 51 females were between 21 to 75 (mean = 42, standard deviation= ± 14) years old. Table (1) is demonstrated the distribution of RA-serological test for patients and control groups.

SPSS (version 17.0) was used for statistical analysis of results. T-test was used to test whether there is a different between control and RA groups. Also, regression, correlation between RA and Anti-chip was tested.

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>RA-patients</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>128</td>
<td>86</td>
<td>42</td>
</tr>
<tr>
<td>Female</td>
<td>172</td>
<td>121</td>
<td>51</td>
</tr>
<tr>
<td>Total</td>
<td>300</td>
<td>207</td>
<td>93</td>
</tr>
<tr>
<td>The age mean(±SD*)</td>
<td>43 (±14)</td>
<td>43(±14)</td>
<td>42 (±14)</td>
</tr>
<tr>
<td>The age range</td>
<td>18-77</td>
<td>18-77</td>
<td>21-75</td>
</tr>
</tbody>
</table>

*SD=Standard Deviation

Results

The results showed that the ACCP increased with the age in male and female patients (A and B in fig 1; table 2; Regression P-value < 0.001, 0.004 respectively). At the same time, the IgA has a positively related with ACCP in male and female patients (Fig 2, A and B; table 2; Regression P-value < 0.001 and 0.001 respectively. On the other hand, the IgM has a positively related with ACCP in female patients (Fig 3, A; table 2; Regression P-value = 0.02). While, male not affected by the change of ACCP (Figure 3, B; table 2; Regression P-value > 0.05).

![Figure (1): A. Log10 of ACCP of Female with age and B. Log10 of ACCP of Male with age.](image-url)
Figure (2): Log10 of ACCP of Female with log10 IgA, and B. Log10 of ACCP of Male with Log10 IgA

Figure (3): Log10 of ACCP of Female with log10 IgM, and B. Log10 of ACCP of Male with Log10 IgM

Table (2): statistical analysis (T-Test, Regression Correlation, and degree of freedom) of study parameters

<table>
<thead>
<tr>
<th>T-Test</th>
<th>P-value</th>
<th>T-Test</th>
<th>P-value</th>
<th>T-Test</th>
<th>P-value</th>
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<tbody>
<tr>
<td></td>
<td>Log10 IgA</td>
<td>Log10 IgM</td>
<td>Log10 IgG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control and RA patient</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RA patient male and female</td>
<td>0.185</td>
<td>0.181</td>
<td>0.009*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control of male and female</td>
<td>0.564</td>
<td>0.957</td>
<td>0.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regression Correlation</td>
<td>df**</td>
<td>P-value</td>
<td>Standard Error</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female Age with ACCP</td>
<td>120</td>
<td>&lt;0.001*</td>
<td>0.0137</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male Age with ACCP</td>
<td>85</td>
<td>0.004*</td>
<td>0.015</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female IgA with ACCP</td>
<td>120</td>
<td>&lt;0.001*</td>
<td>0.08</td>
<td></td>
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</tbody>
</table>
Male IgA with ACCP | 85 | <0.001* | 0.123  
Female IgM with ACCP | 120 | 0.021* | 0.126  
Male IgM with ACCP | 85 | 0.279 | 0.137

*significant < 0.05,  **df: degree of freedom

Figure (4): Error bar present the log10 of IgA, IgM and IgG in control and RA patients.

Discussion
A lot of studies have impeached the magnitude of ACCP testing in differentiation RA from other of inflammatory-diseases [16]. Visser et al [17] found that there was a correlation between arthritis and ACCP. Kastbom et al [18] find that there was a correlation between ACCP and the higher erythrocyte sedimentation rate and C-reactive protein. As well, there was a correlation between rheumatoid factor and increased Erythrocyte sedimentation rate and C-reactive protein. Also, ACCP and rheumatoid factor were closely correlated in a Forslind group study [19]. American Rheumatism Association recommended (ARA) that only the IgM detection in serum as a marker of RA diagnostic criteria [11]. The results also showed that there was a significant change in the values of IgA, IgM and IgG compared with control (Figure4; table 2; T-Test P-value < 0.001). There was no difference of IgA and IgM values in male and female patients while there was a different from IgG values in male compared with female (T-Test P-value < 0.005), so our study was agreed with ARA. Also, the present study finds that there is decreasing in IgG with increasing of ACCP (table 2) and that could be a good indication of RA.

Conclusions
This study concluded that the studied factors could be a good indicator of RA diagnosis in the future for early diagnosis of rheumatoid arthritis.

Acknowledgment
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Author’s contribution
Mrs. Rawaa Behlul Al-Fatlawi conception the research, design and preparation of manuscript, Dr. Huda Ghazi Al-Mashhadi data acquisition, data Analysis and preparation of manuscript, Dr. Wasan Sami Hameed design and preparation of manuscript and providing the clinical details of the cases., Dr. Taghreed Dheyaa Aljazaerioorganizing and reviewed the manuscript.

Conflict of interest
The authors declare no conflict of interest.
References